

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:	Berndl et al.	Docket No.:	49860
Serial No.:	09/937,313	Confirmation No.:	8414
Filing Date:	9/24/2001	Examiner:	YOUNG, MICAH PAUL
Customer No.:	26474	Art Unit:	1618

For: Solubilizing aids in powder form for solid pharmaceutical presentation forms

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Appeal Brief under 37 C.F.R. § 41.37

Sir:

This is an appeal from the Examiner's final rejection of Claims 10 – 12 and 14 – 28, dated October 23, 2006. Claims 10 – 12 and 14 – 28 are currently pending.

The fee set forth in 37 C.F.R. § 41.20(b)(2) is paid by credit card. Form PTO-2038 is enclosed. Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees, to Deposit Account 14.1437. Please credit any excess fees to such account.

Respectfully submitted,
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Real party in interest:

The real party in interest is BASF Aktiengesellschaft, of Ludwigshafen, Germany.

Related appeals and interferences:

To the best of the undersigned's knowledge, there are no related interferences or judicial proceedings.

Status of claims:

- Claims 1 – 9 and 13 are canceled.
- Claims 10 – 12 and 14 – 28 are pending in the application.
- Claims 10 – 12 and 14 – 28 stand rejected.
- Claims 10 – 12 and 14 – 28 are being appealed.

Status of amendment:

No amendments were filed subsequent to the final rejection of October 23, 2007.

Summary of claimed subject matter:

The independent claims involved in the appeal are claims 10, 22, and 25. All other claims are dependent on claim 10, 22 or 25. Summary of the subject matter of the dependent claims is omitted as unnecessary.

The independent claims are directed to processes for producing “solubilizing excipients”¹ in the form of “free-flowing powders”² “for use in solid pharmaceutical presentations, comprising a pharmaceutically acceptable polymer and a liquid or

¹ Page 1, indicated lines 1 – 2 of the present specification.

² Page 4, indicated lines 20 – 21 of the present specification.

semisolid solubilizing surface-active substance.”³ The excipients can be produced either by spray-drying a solution comprising the surface-active substance and the pharmaceutically acceptable polymer or by processing the polymer and the surface-active substance in an extruder to obtain a homogeneous melt and subsequently converting the melt into the free-flowing powder.⁴ All of the independent claims require the pharmaceutically acceptable polymer to be a homo- or copolymer of N-vinylpyrrolidone, which is a water-soluble polymer with Fikentscher K values of from 12 to 1000.⁵ Moreover, all of the independent claims require the surface-active substance to be a liquid or semisolid solubilizing surface-active substance and to be present in the excipient in an amount of from 10 to 50% by weight, based on the total weight of the excipient.⁶ Independent claims 22 and 25, further state that the surface active substance is to be present in a suitable concentration to keep the excipient free flowing. Independent claim 25 further requires the excipient to comprise a liquid that is combined with the powdered excipient.⁷ Finally, claim 10 uses the transitional phrase “consists essentially of,” stating that the excipient produced by the claimed process consists essentially of the particular pharmaceutically acceptable polymer and the particular weight percentages of the surface-active substances.

Grounds of rejection to be reviewed on appeal

Whether the examiner erred in rejecting:

- I. Claims 10 – 12, 14, 17 – 27 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865) and Guzi Jr. et al. (US 4,127,422)
- II. Claims 15 and 16 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865), Shih et al. (US 6,011,096) and Sutton et al. (US 5,993,805)

³ Page 1, indicated lines 7 – 10 of the present specification.

⁴ Page 3, indicated lines 30 – 46 of the present specification.

⁵ Page 3, indicated lines 15 – 21 of the present specification.

⁶ Page 2, indicated lines 9 – 25 of the present specification.

⁷ Page 4, indicated lines 38 – 42 of the present specification.

Argument

The United States Supreme Court in *Graham v. John Deere*, 383 U.S. 1, 148 USPQ 459 (1966) held that “[u]nder §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.”⁸ Thus, four factual inquiries must be addressed to determine obviousness:

- (A) the scope and contents of the prior art;
- (B) the differences between the prior art and the claims in issue;
- (C) the level of ordinary skill in the pertinent art; and
- (D) evidence of secondary considerations.

With regard to (A), (B) and (C) the United States Supreme Court in *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ____ (2007) stated that “[o]ften, it will be necessary ... to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine known elements in the fashion claimed by the patent at issue.”⁹

Appellants’ invention is directed to a process for producing specifically formulated free-flowing, powder excipients for use in a solid pharmaceutical dosage form. “Once [appellants] had taught how this could be done, the redesign may, by hindsight, seem to be obvious to one having ordinary skills in the ... art. However, when viewed as of the time [appellants’] invention was made, and without the benefit of [appellants’] disclosure ... nothing in the art of record ... suggests [appellants’]

⁸ *Graham v. John Deere*, 383 U.S. 1, at 17 – 18, 148 USPQ 459 (1966).

⁹ *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ____ (2007), Slip op. at 14.

invention].”¹⁰

I. Rejection of claims 10 – 12, 14, 17 – 27 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865) and Guzi Jr. et al. (US 4,127,422)

The examiner erred in rejecting claims 10 – 12, 14, 17 – 27 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865) and Guzi Jr. et al. (US 4,127,422). The rejection cannot be maintained when the cited references are properly considered from the standpoint of a person of ordinary skill in the art at the time appellants’ invention was made. Moreover, the rejection cannot be maintained from any logical standpoint, when the cited references are considered in their entireties, including portions which teach away from appellants’ invention.

(A) Discussion of the Ball et al. reference:

It is true enough that searching the Ball et al. reference for terms used in appellants’ claims, such as, “excipient,” “surfactant,” “polyvinylpyrrolidone,” and “K-value” yields some matches. The terms are, indeed, mentioned in the reference. However, “[a] person of ordinary skill is ... not an automaton[.]”¹¹ and would have sought to understand the technical relationship between these terms. In so doing, a skilled artisan would have understood that the Ball et al. reference relates to the preparation of a powdery cross-linkable composition intended for application in building compositions or as binders for paper. A skilled artisan would have recognized that water-soluble compositions would not be useful as building compositions or as binders for paper, and thus would not have been surprised that Ball et al. includes a water insoluble polymer.

A skilled artisan would also have noticed that “[t]he water-insoluble polymers a) are preferably prepared using the emulsion polymerization process.”¹² Since the polymer is obtained from equally water insoluble monomers like dienes, olefins, vinyl esters and

¹⁰ *In re Ratti*, 270 F.2d 810, 123, 123 USPQ 349 at 352 (C.C.P.A. 1959).

¹¹ *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ____ (2007), Slip op. at 17.

¹² Column 5, indicated lines 52 – 53 of US 6,063,865.

the like (See: Column 2, lines 29 – 46 of US 6,063,865) the emulsion polymerization is carried out in the presence of emulsifiers. It should be noted that these emulsifiers are not required components of the final Ball et al. formulation; the emulsifiers are used only when component a) is prepared by the preferred method, i.e. by emulsion polymerization. Moreover, the examiner has not established that these emulsifiers would ever be incorporated into Ball et al.'s final product, a crosslinkable powder composition.

At any rate, Ball et al. make clear that “it is possible to use all emulsifiers customarily employed in emulsion polymerization. Suitable emulsifiers include anionic, cationic and also nonionic emulsifiers. The emulsifiers are preferably used in an amount of up to 6% by weight, based on the total weight of the monomer.”¹³

Thus, a skilled artisan would have understood that the emulsifiers were only meant to be present during formation of the water insoluble polymer a) by emulsion polymerization, and that later the resulting dispersion of water insoluble polymer a) can be spray-dried in the presence of a protective colloid such as the water soluble polymer b), e.g., polyvinyl pyrrolidone. Indeed, Ball et al. make clear that their “invention provides a crosslinkable powder composition which ... comprises a) from 30 to 95 parts by weight of one or more water-insoluble, film-forming polymers ... b) from 5 to 70 parts by weight of one or more water-soluble polymers ... [and] c) one or more compounds containing at least two functional groups which are present in salt form ...”¹⁴ In other words, a skilled artisan would have understood that the Ball et al. reference is not directed to an excipient comprising a surfactant, but to a crosslinkable powder composition comprising a water-insoluble polymer, wherein the water-insoluble polymer may be formed by emulsion polymerization in the presence of an emulsifier.

The rejection is, of course, based on a combination of references. However it is helpful at this point to compare the Ball et al. reference to the claimed invention. Such a comparison makes clear that the reference fails to teach or suggest an excipient comprising from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance. Since the Ball et al. reference is not directed to an excipient comprising a surfactant, but to a crosslinkable powder

¹³ Column 6, indicated lines 4 – 8 of US 6,063,865.

¹⁴ Column 2, indicated lines 7 – 25 of US 6,063,865.

composition comprising a water-insoluble polymer, which may be formed by emulsion polymerization in the presence of an emulsifier, the reference does not teach this claim limitation.

Ball et al. make clear that “[t]he emulsifiers are preferably used [in the emulsification polymerization of component a)] in an amount of up to 6% by weight based on the total weight of the monomers.”¹⁵ Ball et al. provides no apparent reason to increase the concentration of surfactant beyond the preferred maximum concentration for use in the emulsification polymerization of component a). Moreover, even if:

- (1) polymer a) is prepared by emulsion polymerization,
- (2) the emulsion polymerization of polymer a) is carried out in the presence of emulsifiers,
- (3) the maximum preferable amount of emulsifiers is used in the emulsion polymerization of polymer a), and
- (4) all of the emulsifiers used in the emulsion polymerization of polymer a) were somehow¹⁶ incorporated into the crosslinkable powder composition, after the polymer a) dispersion is spray-dried,

the emulsifiers would make up only 5.7% by weight,¹⁷ of the crosslinkable powder composition. Thus, the Ball et al. reference clearly fails to teach or suggest an excipient comprising from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance.

(B) Discussion of the Guzi, Jr. et al. reference:

The Guzi, Jr. et al. reference “relates to dry pigment compositions in water-dispersible form....”¹⁸ “The invention can be practiced with the inorganic and organic

¹⁵ US 6,063,865, col. 6, indicated lines 7 – 9 (emphasis added).

¹⁶ The examiner has not established that any of the emulsifiers would be incorporated into the crosslinkable powder composition.

¹⁷ Ball et al.'s crosslinkable powder composition comprises from 30 to 95 parts by weight of component a), which, if prepared by emulsion polymerization, includes at most 6% by weight of emulsifier. Thus, assuming for the sake of argument that 100% of the emulsifier finds its way into the crosslinkable powder composition, the emulsifier could theoretically make up from 1.8% to a maximum of 5.7% of the crosslinkable powder composition.

¹⁸ Column 1, indicated lines 10 – 11 of US 4,127,422.

prime pigments, extender pigments, metallic pigments, the various finely divided channel and furnace blacks and the like.”¹⁹ The reference describes typical pigments that are suitable for use in the dry pigment compositions,²⁰ but stresses that “[i]t is of course understood and appreciated that all pigments do not behave in the same manner in a given system and that for each pigment there will be an optimum concentration.”²¹ Guzi, Jr. et al. emphasize that “[w]ithin the scope of the present invention it has been found that compositions containing high concentrations of pigment can be produced.” Accordingly, Guzi, Jr. et al. disclose a two step process comprising the steps of:

forming a homogeneous mixture comprising

milled or homogenized pigment,

water, and ...

from 15 to 45% [by weight of the pigment] of a non-ionic dispersing agent ...

from 10 to about 67% [by weight of the pigment] of at least one water-dispersible nonionic polymer ... and

from 0 to about 40% [by weight of the pigment] of a nonionic colloid ... and

removing the water from said mixture until a dry composition is obtained ... the total amount of dispersing agent, polymer and colloid being from 20 to 45% by weight of the dry composition.²²

The following table illustrates possible compositions of Guzi, Jr. et al.’s dry pigment composition.

¹⁹ Column 2, indicated lines 59 – 62 of US 4,127,422.

²⁰ See: Column 2, indicated line 62 – column 3, indicated line 2 of US 4,127,422.

²¹ Column 2, indicated line 10 – 13 of US 4,127,422.

²² Column 2, indicated lines 26 – 44 of US 4,127,422 (emphasis added).

	Parts by weight of Dry Pigment Composition with Minimum Dispersing Agent (15% by weight of pigment)	Parts by weight of Dry Pigment Composition with Maximum Dispersing Agent (45 % by weight of pigment)
Pigment (parts by weight):	100	100
Dispersing (parts by weight):	15	45
Polymer (parts by weight):	67	10
Colloid (parts by weight):	0	0
Total (parts by weight):	182	155
Total amount of dispersing agent, polymer and colloid by weight of the dry composition (must be from 20 to 45%):	45%	35%
Amount of dispersing agent in the dry composition	8%	29%

This table illustrates that the weight percentages of pigment (from 15 to 45%) given for the amount of dispersing agent utilized in the process disclosed by the Guzi, Jr. et al. reference are not the minimum and maximum weight percentages of dispersing agent in the dry pigment composition that is produced by the process. Indeed, the Guzi, Jr. et al. reference is focused on ensuring that “[dry pigment] compositions containing high concentrations of pigment [are] produced....”²³ The Guzi Jr. et al. reference teaches that despite the risk of detriment to other desirable properties a “sufficient [amount of] dispersing agent must be present to provide ease of processing and particle size reduction.”²⁴ More specifically, the reference teaches that “[u]sually, an amount between about 15 and 35% [of dispersing agent] by weight of the pigment will provide good dispersibility without detriment to any other desirable properties.”²⁵

Guzy, Jr. et al. also stress that “[t]he practice of the invention also requires the presence of from 10% to about 67% by weight of the pigment of a water-dispersible nonionic polymer which is either an at least partially hydrolyzed polymer of vinyl

²³ Column 2, indicated lines 15 – 16 of US 4,127,422.

²⁴ Column 3, indicated lines 46 – 48 of US 4,127,422.

²⁵ Column 3, indicated lines 48 – 51 of US 4,127,422.

acetate, a polymer of an N-vinyl pyrrolidone or mixtures thereof.”²⁶ Guzi, Jr. et al. make clear that “The function of the polymer is multiphase since it:

- [1] acts synergistically with the dispersing agent to reduce the pigment particle size beyond that which can be accomplished by the dispersing agent alone,
- [2] acts as a coating for the pigment particles to prevent reagglomeration during the drying process,
- [3] acts to prevent flocculation and provides broad compatibility in a broad variety of aqueous systems.”²⁷

In other words, Guzi, Jr. et al. put a clear emphasis on the water-dispersible nonionic polymer not on the dispersing agent. The dispersing agent merely “provide[s] ease of processing and [pigment] particle size reduction.”²⁸ Moreover, the reference makes clear that when used alone the dispersing agent cannot reduce the pigment particle size as effectively as when used in combination with the water-dispersible nonionic polymer.

(C) Discussion of the proposed combination of the Ball et al. reference and the Guzi, Jr. et al. reference:

Since the present rejection is based on a combination of the disclosures of Ball et al. and Guzi, Jr. et al., appellants now turn to an analysis of whether a skilled artisan at the time appellants’ invention was made would have found it obvious to combine the references or to modify the Ball et al. reference based on the teachings of Guzi, Jr. et al.

As previously noted, since the Ball et al. reference is not directed to an excipient comprising a surfactant, but to a crosslinkable powder composition comprising a water-insoluble polymer, which may be formed by emulsion polymerization in the presence of an emulsifier (or by other methods that need not involve an emulsifier at all), the reference fails to teach or suggest an excipient comprising from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance.²⁹ In other words, the Ball et al. reference makes clear that emulsifiers

²⁶ Column 3, indicated lines 52 – 57 of US 4,127,422.

²⁷ Column 3, indicated lines 57 – 64 of US 4,127,422.

²⁸ Column 3, indicated lines 47 – 48 of US 4,127,422.

²⁹ Please note: the “consisting essentially of” terminology of claim 10 and the additional limitations of

are used as dispersants in the emulsification polymerization of water-insoluble polymer a) and assigns no importance to the emulsifiers after the formation of water-insoluble polymer a). Ball et al. do not teach or suggest that emulsifiers serve any purpose in the subsequent step of spray-drying the dispersion of polymer a), or as components in the cross-linkable powder composition that results from the process.

Again, the examiner has not established that any of the emulsifiers would ever be incorporated into the final product. However, as discussed above, even if polymer a) is prepared by emulsion polymerization, the emulsion polymerization is carried out in the presence of emulsifiers, (3) the maximum preferable amount of emulsifiers is used, and (4) all of the emulsifiers were somehow incorporated into the crosslinkable powder composition, the emulsifiers would make up only 5.7% by weight,³⁰ of the crosslinkable powder composition.

Since the Guzi, Jr. et al. reference does not even involve an emulsion polymerization, it should be quite clear that the Guzi, Jr. et al. reference could not have provided a skilled artisan with an apparent reason to increase the weight percentage of emulsifier for use in the emulsion polymerization of component a) according to the Ball et al. reference.

The dispersing agent in Guzi, Jr. et al. is only discussed in the context of the step wherein a pigment dispersion is formed. In this step, either (1) "all of the ingredients ... are milled or homogenized conventionally[,]"³¹ or (2) "an aqueous dispersion of the pigment is first produced by milling or homogenizing the pigment in water in the presence of the nonionic dispersing agent ... and then the pigment dispersion so produced is intimately mixed ... with the desired amount of the water-dispersible nonionic polymer and colloid, if employed."³² The dispersing agent merely "provide[s] ease of processing and [pigment] particle size reduction."³³ Such milling would seem to be unnecessary

claims 22 and 25 will be discussed later.

³⁰ Ball et al.'s crosslinkable powder composition comprises from 30 to 95 parts by weight of component a), which, if prepared by emulsion polymerization, includes at most 6% by weight of emulsifier. Thus, assuming for the sake of argument that 100% of the emulsifier finds its way into the crosslinkable powder composition, the emulsifier could theoretically make up from 1.8% to a maximum of 5.7% of the crosslinkable powder composition.

³¹ Column 5, indicated lines 26 – 29 of US 4,127,422.

³² Column 5, indicated lines 32 – 39 of US 4,127,422.

³³ Column 3, indicated lines 47 – 48 of US 4,127,422.

where Ball's water-insoluble polymer or crosslinkable powder is concerned, since the Ball et al. reference makes clear that, if the disclosed process is employed, the dispersion of polymer a) to be spray-dried will have a "mean particle size ... from 0.1 to 10 μm , preferably from 0.2 to 5 μm ."³⁴ Thus, Guzi, Jr. et al. provided no apparent reason to contrive a way to incorporate dispersing agent into the solution that Ball et al. spray-dry.

In summary, it seems that without the requisite explicit analysis,³⁵ the examiner has cursorily concluded that "[a]n artisan would have been motivated to include the surfactants of [Guzi, Jr. et al.] into the [Ball et al.] process in order to ease production and reduction of the particles."³⁶ Yet, when an explicit analysis is made, it is readily apparent that Guzi, Jr. et al. provided no teaching, suggestion, motivation or apparent reason to contrive a way to incorporate more dispersing agent into the solution that Ball et al. spray-dry. Thus, the present rejection is in error.

II. Rejection of claims 15 and 16 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865), Shih et al. (US 6,011,096) and Sutton et al. (US 5,993,805)

The examiner also erred in rejection claims 15 and 16 under 35 U.S.C. §103(a) over Ball et al. (US 6,063,865), Shih et al. (US 6,011,096) and Sutton et al. (US 5,993,805). Both claims 15 and 16 depend from claim 10. Thus, both claims 15 and 16 include the limitation that the excipient consists essentially of a particular pharmaceutically acceptable polymer and from 10 to 50% by weight, based on the total weight of said excipient, of a liquid or semisolid solubilizing surface-active substance. The secondary references were not cited to provide an apparent reason to modify the teaching of Ball et al. to provide the claimed weight percentage of surface-active substance. Thus, the rejection is in error.

III. Conclusion

³⁴ Column 6, indicated lines 36 – 37 of US 6,063,865.

³⁵ *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ____ (2007), Slip op. at 14.

³⁶ Page 4, lines 1 – 3 of the Office action of October 23, 2006.

Since the rejections are in error, Appellants respectfully request that the rejections be reversed.

Claims appendix.

- 1-9 (canceled).
10. (previously presented) A process for producing an excipient adapted for use in a solid pharmaceutical dosage form, wherein said excipient is in the form of a free-flowing powder and consists essentially of
- a pharmaceutically acceptable polymer and
 - from 10 to 50% by weight, based on the total weight of said excipient, of a liquid or semisolid solubilizing surface-active substance, wherein
 - the polymer in the excipient is a homo- or copolymer of N-vinylpyrrolidone, which is a water-soluble polymer with
 - Fikentscher K values of from 12 to 100; which comprises
 - either spray-drying a solution comprising the surface-active substance and the pharmaceutically acceptable polymer, or
 - processing the polymer and the surface-active substance in an extruder to obtain a homogeneous melt and subsequently converting the melt into the free-flowing powder.
11. (previously presented) The process according to claim 10, wherein the excipient comprises a surface-active substance which has a drop point in the range from 20 to 40°C.
12. (previously presented) The process according to claim 10, wherein the excipient comprises a surface-active substance which has an HLB of from 10 to 15.
13. (canceled)
14. (previously presented) The process according to claim 10, wherein the excipient comprises from 15 to 40% by weight of the surface-active substance.

15. (previously presented) The process according to claim 10, wherein the excipient comprises ethoxylated sorbitan fatty acid esters as surface-active substances.
16. (previously presented) The process according to claim 10, wherein the excipient comprises the products of the reaction of ethylene oxide with castor oil, hydrogenated castor oil or with 12-hydroxystearic acid as surface active substance.
17. (previously presented) The process according to claim 10, wherein the excipient comprises from 20 to 30% by weight of the surface-active substances.
18. (previously presented) The process according to claim 10, wherein the excipient is in the form of a free-flowing powder of particles having a particle size of from 10 to 1000 μ .
19. (previously presented) A solubilizer-containing powder comprising the excipient obtained by the process of claim 10 and optionally one or more ingredients selected from the group consisting of flow regulators, dyes, mold release agents, fats, waxes, disintegrants, bulking agents and other tableting excipients.
20. (previously presented) The process according to claim 10, wherein the surface-active substance of the excipient is a non-ionic compound.
21. (previously presented) The process of claim 10, wherein said excipient is free of pigment.
22. (previously presented) A process for producing a free-flowing powder excipient for use in a solid pharmaceutical dosage form comprising:
 - a pharmaceutically acceptable polymer, and
 - from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance, wherein

the pharmaceutically acceptable polymer in the excipient is a homo- or copolymer of N-vinylpyrrolidone, and is a water-soluble polymer with Fikentscher K values of from 12 to

100

the process comprising producing the free-flowing powder excipient by one of:
spray-drying a solution comprising the surface-active substance and the pharmaceutically acceptable polymer, or
extruding the polymer and the surface-active substance to obtain a homogeneous melt and subsequently converting the melt into the free-flowing powder, wherein
the surface active substance is in a suitable concentration to keep the excipient free flowing.

23. (previously presented) The process of claim 22, wherein the concentration of surface active substance is 15 to 40% by weight based on the weight of the excipient.
24. (previously presented) The process of claim 22, wherein the concentration of surface active substance is 20 to 30% by weight based on the weight of the excipient.
25. (previously presented) A process for producing a free-flowing powder excipient for use in a solid pharmaceutical dosage form comprising:
a pharmaceutically acceptable polymer,
a liquid, and
from 10 to 50% by weight, based on the total weight of the excipient, of a liquid or semisolid solubilizing surface-active substance, wherein
the pharmaceutically acceptable polymer in the excipient is a homo- or copolymer of N-vinylpyrrolidone, and
is a water-soluble polymer with Fikentscher K values of from 12 to

100

the process comprising producing the free-flowing powder excipient by one of:
spray-drying a solution comprising the surface-active substance and the
pharmaceutically acceptable polymer, or
extruding the polymer and the surface-active substance to obtain a
homogeneous melt and subsequently converting the melt into the free-
flowing powder, wherein
the surface active substance is in a suitable concentration to keep the excipient
free flowing, and wherein
the liquid is combined with the powdered excipient.

26. (previously presented) The process of claim 25, wherein the concentration of surface active substance is 15 to 40% by weight based on the weight of the excipient.
27. (previously presented) The process of claim 25, wherein the concentration of surface active substance is 20 to 30% by weight based on the weight of the excipient.
28. (previously presented) The process of claim 25, wherein the liquid is an oil.

Evidence appendix

None.

Related proceedings appendix

None.